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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/779,724	02/18/2004	K. S. Keshava Murthy	PT2074001	1109

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EXAMINER

BALLS, ROBERT J

ART UNIT PAPER NUMBER

1625

DATE MAILED: 10/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

10/779,724

Applicant(s)

MURTHY ET AL.

Examiner

R. James Balls

Art Unit

1625

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 28 August 2006.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-32 is/are pending in the application.
- 4a) Of the above claim(s) 23-25 and 27-32 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-22 and 26 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 6/02/2004.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_.

### DETAILED ACTION

1. Claims 1-32 are pending.

#### *Priority*

2. Receipt is acknowledged of a certified copy of a foreign application, CANADA 2,457,459. If this copy is being filed to obtain the benefits of the foreign filing date under 35 U.S.C. 119(a)-(d), applicant should also file a claim for such priority as required by 35 U.S.C. 119(b). If the application being examined is an original application filed under 35 U.S.C. 111(a) (other than a design application) on or after November 29, 2000, the claim for priority must be presented during the pendency of the application, and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior foreign application. See 37 CFR 1.55(a)(1)(i). If the application being examined has entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the claim for priority must be made during the pendency of the application and within the time limit set forth in the PCT and Regulations of the PCT. See 37 CFR 1.55(a)(1)(ii). Any claim for priority under 35 U.S.C. 119(a)-(d) or (f) or 365(a) or (b) not presented within the time period set forth in 37 CFR 1.55(a)(1) is considered to have been waived. If a claim for foreign priority is presented after the time period set forth in 37 CFR 1.55(a)(1), the claim may be accepted if the claim properly identifies the prior foreign application and is accompanied by a grantable petition to accept an unintentionally delayed claim for priority. See 37 CFR 1.55(c).

The Application Data Sheet and the Oath or Declaration both refer to a Canadian application filed on February 11, 2004, but neither document identifies the Canadian application number, i.e. CANADA 2,457,459. 35 U.S.C. §119(b) requires that claim to priority be made identifying the foreign application by specifying the application number. Accordingly, the instant case is not entitled to the foreign priority date.

### ***Election/Restrictions***

3. Applicant's election without traverse of Group II (Claims 1-22 and 26) in the reply filed on August 26, 2006 is acknowledged.
4. Claims 1-22 and 26 are under examination. Claims 23-25 and 27-32 are withdrawn as being directed to non-elected subject matter.

### ***Claim Rejections - 35 USC § 112, Second Paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. §112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 2-7, 9, 11-15 and 18-22 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "polar" and "non-polar" in claims are relative terms not defined by the claims and the specification does not provide a standard for ascertaining the requisite degree. These terms are ambiguous because there is no uniform definition delineating whether a particular

solvent belongs to one of these groups. The specification on page 7, paragraph 28 provides examples of how applicants categorize a limited number of preferred solvents but the present claims are not limited to the preferred solvents. Therefore, one of ordinary skill in the art would not be reasonably appraised of the metes and bounds of the claims. It is recommended that applicants amend the claim to positively recite the intended solvents by, for example, including the solvents recited in the specification on page 7, paragraph 28. At present, the claims are given their broadest reasonable interpretation and considered to include all solvents.

***Claim Rejections - 35 USC § 102(b)***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-2, 10-11 and 16-17 are rejected under 35 U.S.C. §102(b) as being anticipated by Herbert et al., *Clopidogrel Hydratesulfate*, DRUGS OF THE FUTURE, 18(2):107-112 (1993). The specification on page 4, lines 11-13 refer to this article and allege the text of the flowsheet on page 108 of the article erroneously designates use of the dextro camphorsulfonic acid. It is not clear why applicants consider the flowsheet to contain an error, as the "Synthesis" section of the article on page 107 also designates use of the dextro camphorsulphonic acid. See page 107, "Synthesis", 2(b).

7. Claims 1-2, 10-11 and 16-17 are rejected under 35 U.S.C. §102(b) as being anticipated by Pandey et al. (US Patent No. 6,635,763). Example 33 discloses resolving racemic clopidogrel with (1S)-(+)-camphor-10-sulphonic acid in an ethyl acetate/water solution.

***Claim Rejections - 35 USC § 103(a)***

The following is a quotation of 35 U.S.C. §103(a), which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 1-5, 10-13 and 16-20 are rejected under 35 U.S.C. §103(a) as being unpatentable over Pandey et al. (US Patent No. 6,635,763).

**Determination of the Scope and Content of the Prior Art (MPEP §2141.01)**

Pandey et al. shows resolution of racemic clopidogrel using a resolving agent (S)-10-camphorsulfonic acid. See Example 33 and Claim 16. See Column 12, lines 15-19 for suitable solvents useable in the resolution procedure.

**Ascertainment of the Difference Between the Prior Art and the Claims (MPEP §2141.02)**

The instant claims differ from Pandey et al. by requiring a specific species (solvents) selected from the prior art genus. The prior art discloses the individual species (solvents) required in the instant claims. See Column 12, lines 15-19. Useable solvents include (C1-C4)ketones and methyl ethyl ketone and Example 33 specifically uses acetone.

**Motivation and Prima Facie Obviousness-Rationale (MPEP §§2142-2143)**

It would have been obvious to one having ordinary skill in the art at the time of the invention to select any of the species (solvents) of the genus taught by the prior art

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reference because an ordinary artisan would have the reasonable expectation that any of the species (solvents) would have similar properties and, thus, the same use as the genus as a whole.

### ***Claim Rejections - 35 USC § 103(a)***

The following is a quotation of 35 U.S.C. §103(a), which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. Claims 6-7, 14-15 and 21-22 are rejected under 35 U.S.C. §103(a) as being unpatentable over Pandey et al. (US Patent No. 6,635,763) in view of Valeriano et al. (US Patent No. 6,737,411).

#### **Determination of the Scope and Content of the Prior Art (MPEP §2141.01)**

Pandey et al. shows resolution of racemic clopidogrel using a resolving agent (S)-10-camphorsulfonic acid. See Example 33 and Claim 16. See Column 12, lines 15-19 for suitable solvents useable in the resolution procedure.

Valeriano et al. teach using toluene as the solvent in the resolution of clopidogrel. See column 12, Example 4.

#### **Ascertainment of the Difference Between the Prior Art and the Claims (MPEP §2141.02)**

Pandey et al. does not teach using the particular solvent toluene. Valeriano et al. teach using the solvent toluene but use the resolving agent (R)-10-camphorsulfonic acid instead of (S)-10-camphorsulfonic acid.

#### **Motivation and Prima Facie Obviousness-Rationale (MPEP §§2142-2143)**

One of ordinary skill in the art would be motivated to use the solvent toluene in the resolution of clopidogrel because solvents useable in resolution using (R)-10-camphorsulfonic acid are also useable in resolution using (S)-10-camphorsulfonic acid as demonstrated by Pandey et al. Pandey et al. provides motivation to combine the references by showing that changing from (R) to (S)-10-camphorsulfonic acid does not require a change in solvents. See Examples 33 and 34 where the same solvent, ethyl acetate, was used with both (S) and (R)-10-camphorsulfonic acid as the resolving

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agent. Therefore, one of ordinary skill in the art would expect that toluene, which was useable with (R)-10-camphorsulphonic would also be useable with (S)-10-camphorulphonic acid.

### ***Claim Rejections - 35 USC § 103(a)***

The following is a quotation of 35 U.S.C. §103(a), which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claims 8-9, are rejected under 35 U.S.C. §103(a) as being unpatentable over Pandey et al. in view of Cheronis, SEMIMCRO EXPERIMENTAL ORGANIC CHEMISTRY, 31-49 (J. de Graff 1958).

#### **Determination of the Scope and Content of the Prior Art (MPEP §2141.01)**

Pandey et al. shows resolution of racemic clopidogrel using a resolving agent (S)-10-camphorsulfonic acid and explains that by repeated crystallization from a suitable solvent, the desired diastereomer can be procured. See column 12, lines 28-31.

Cheronis shows that purification by recrystallization is routine and well known in the art. See Chapter 5, pages 31-49.

#### **Ascertainment of the Difference Between the Prior Art and the Claims (MPEP §2141.02)**

Pandey et al. does not show a purity of about 99.5% as required by Claim 8.

#### **Motivation and Prima Facie Obviousness-Rationale (MPEP §§2142-2143)**

One of ordinary skill in the art would be motivated to purify the stereoisomer of Claims 8-9 by way of crystallization because recrystallization is a well-known and effective procedure used for purification. Chiron writes that organic compounds can be purified by means of crystallization. See page 31, first paragraph. In terms of the degree of purity, the MPEP explains that optimization of concentration by means of routine experimentation is not patentable absent unexpected results. See 2144.05, Optimization of Ranges.



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In terms of solvent selection, Pandey et al. describes using methyl ethyl ketone for the crystallization of clopidogrel (as claimed in Claim 9). See column 12, line 18. Also, Chiron explains that the solvent should dissolve an appreciable amount of the product when hot and specifically lists toluene (as claimed in Claim 9) as a common solvent for organic crystallization. See Table 5-1 on page 33.

### ***Claim Rejections - 35 USC § 103(a)***

The following is a quotation of 35 U.S.C. §103(a), which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. Claim 26 is rejected under 35 U.S.C. §103(a) as being unpatentable over Pandey et al. (US Patent No. 6,635,763) or Herbert et al., *Clopidogrel Hydratesulfate*, DRUGS OF THE FUTURE, 18(2):107-112 (1993) in view of Cheronis, SEMIMICRO EXPERIMENTAL ORGANIC CHEMISTRY, 31-49 (J. de Graff 1958).

#### **Determination of the Scope and Content of the Prior Art (MPEP §2141.01)**

Pandey et al. shows resolution of racemic clopidogrel using a resolving agent (S)-10-camphorsulfonic acid. See Example 33 and Claim 16.

Herbert et al. also shows the resolution of racemic clopidogrel using a resolving agent (S)-10-camphorsulfonic acid. See page 107, "Synthesis", 2(b).

Cheronis explains that seeding is a commonly used technique in crystallization. See page 42, first full paragraph.

#### **Ascertainment of the Difference Between the Prior Art and the Claims (MPEP §2141.02)**

Pandey et al. and Herbert et al. do not provide an additional step of seeding as required by Claim 26.

#### **Motivation and Prima Facie Obviousness-Rationale (MPEP §§2142-2143)**

One of ordinary skill in the art would be motivated to employ the step of seeding in the recrystallization of clopidogrel because it is a common and well-recognized technique to ensure crystal formation. See Cheronis, page 42, first full paragraph.


**Conclusion**

12. No claims are allowed.
13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to R. James Balls whose telephone number is (571) 272-7997. The examiner can normally be reached on Mon - Fri 8:00am - 4:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tom McKenzie can be reached on (571) 272-0670. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

R. James Balls  
October 14, 2006

  
Celia Chang  
Primary Examiner  
Art Unit 1625